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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,229	06/25/2003	Narendra S. Yadav	CL1127 US DIV	5578

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EXAMINER

ZHENG, LI

ART UNIT PAPER NUMBER

1638

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/603,229

Applicant(s)

YADAV ET AL.

Examiner

Li Zheng

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/25/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>6252003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities:

A U.S. application serial number, 09/442,021, is recited on page 1, the 1st paragraph after the title (See specification amendments filed on 6/25/2003) . The status of the application should be updated. If the application was allowed, please insert the U.S. patent number.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 -36 recite the limitation "The binary transgenic viral expression system of Claim 32" in line 1 of each claim. There is insufficient antecedent basis for this limitation in the claim since claim 32 is drawn to a binary transgenic expression system.

In claims 33-36, the recitation, "binary transgenic viral expression system", in line 1 renders the claims indefinite. There is no definition for this term in specification and it is not clear what is encompassed by such system. The metes and bounds are not clear. For examination purpose, this term does not set any limitation to the claims. It is noted that a binary viral expression system defined on page 20, lines 20-35 contains an inactive replicon which may comprise target gene. Therefore, it is suggested the instant claims be drawn to a binary viral expression system. Clarification is required.

Further, in claim 35, the recitation, "PI-HC-Pro, HC-Pro and 2b protein", renders the claim indefinite. It is unclear what genes they represent. It is suggested to be replaced with –P1-HC-Pro and HC-Pro polypeptides of Tobacco Etch Virus and 2b protein of Cucumber Mosaic Virus--, as described on page 35, last paragraph.

Still further, in claim 32, it is unclear the blocking fragment of i) is inserted into the suppressor of ii), or the suppressor of ii) is within the blocking fragment of i). The metes and bounds are not clear. It is also not clear how the site-specific recombination activates the suppressor gene. Is it by excising the blocking sequence or some other ways? The metes and bounds are not clear.

3. Claims 32-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of the full content of the specification indicates that obtaining silencing suppressor, inactive replicon is essential for the invention.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention “requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” (See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)). The court also concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to “visualize or recognize the identity of the members of the genus.” *Id.*

A review of the language of claims 32-36 indicates that claims are broadly drawn to genera of any silencing suppressors and any inactive replicons. The specification only describes P1-HC-Pro and HC-Pro polypeptides of Tobacco Etch Virus and 2b protein of Cucumber Mosaic Virus (page 35, last paragraph) as silencing suppressors in plant, and inactive replicons from geminiviruses and single-strand RNA viruses (pages 47-50, Example 2 from page 50 and Example 3 from page 54). Neither the specification

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nor the prior art describe the gene silencing suppressors or inactive replicons from other sources or conserved structures for silencing suppressors or inactive replicons, which therefore would be shared among all the species of the claimed genus. The specification does not correlate the function of gene silencing suppressing to the structure of suppressors. Therefore, given the breadth of the claims and the lack of further guidance, a person skilled in the art would conclude that applicant is not in possession of the claimed invention.

6. Claims 32-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for P1-HC-Pro and HC-Pro polypeptides of Tobacco Etch Virus and 2b protein of Cucumber Mosaic Virus (page 35, last paragraph) as silencing suppressors in plant, and inactive replicons from geminiviruses and single-strand RNA viruses, does not reasonably provide enablement for any silencing suppressors or any inactive replicons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claims are broadly drawn towards a binary transgenic viral expression system comprising a chromosomally integrated inactive replicon, derived from any virus, and a chromosomally integrated inactive silencing suppressors transgene, from any source.

The specification, for example on pages 47-50 and 50-54, teaches an inactive replicon based on the geminiviruses ACMV and TGMV as well as single-strand RNA

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virus PVX, and use of these systems to express GUS, GFP or luciferase in transgenic plants. The specification also teaches P1-HC-Pro and HC-Pro polypeptides of Tobacco Etch Virus and 2b protein of Cucumber Mosaic Virus (page 35, last paragraph) as silencing suppressors in plant. However, the specification does not enable inactive replicons based on viruses other than geminiviruses as well as single-strand RNA viruses. Timmermans et al. (Annu. Rev. Plant Physiol. Plant Mol. Biol., 1994, 45:79-112) teach that the mechanism of geminiviral DNA replication distinguishes geminiviruses from all other plant viruses (page 92). Therefore, it is unpredictable that the expression system may be used with any virus other than geminiviruses as well as single-strand RNA viruses. The specification also does not teach silencing suppressors other than P1-HC-Pro and HC-Pro polypeptides of Tobacco Etch Virus and 2b protein of Cucumber Mosaic Virus. In the absence of further guidance, undue experimentation would be required by a person skilled in the art to identify and isolate nucleotide sequences encoding other silencing suppressor. Given claim breadth, unpredictability of the art, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate inactive replicon from any other viruses.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 32 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lloyd et al. (1994, Mol. Gen. Genet.242:653-657) in view of Brigneti et al. (1998, The EMBO Journal 17:6739-6746).

The claims are drawn to a binary transgenic viral expression system comprising 1) a chromosomally integrated blocking fragment bounded by site-specific sequences responsive to a site-specific recombinase; and 2) a chromosomally integrated inactive silencing suppressor transgene; wherein expression of the site specific recombinase results in the site-specific recombination that activates the silencing suppressor gene. Please note that since binary transgenic viral expression system is not given any weight in the claims, the viral replicon is NOT considered as a limitation to the claims.

Lloyd et al. teach use of the FLP/FRT site-specific recombination system in stably transformed tobacco plant. Tobacco plants were transformed with a construct

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comprising 2.8 kb of a space sequence (blocking sequence) flanked by FRT sites, placed between the CaMV 35S promoter and hph gene. Plants were also transformed with a construct comprising both FLP coding sequence operably linked to the CaMV 35S promoter promoter. Plant were either re-transformed with FLP or FRT site-containing plasmid, or crossed, so that plants comprising both FLP coding sequence and FRT sites were generated. Progeny plants were hygromycin resistant, indicating that FLP-mediated recombination removed the 2.8 kb spacer flanked by FRT sites and allowed expressing of the hph gene (page 656).

Lloyd et al. do not teach the silencing suppressor gene.

Brigneti et al. teach HC-Pro polypeptides of TVY and 2b protein of Cucumber Mosaic Virus suppress the post transcriptional gene silencing and allow expression of GFP in the cell (abstract).

It would have been obvious to a person with ordinary skill in the art to modify the construct of Lloyd et al. by replacing the hph gene with 2b protein of CMV of Brigneti et al., resulting in the instant claims. One would have been motivated to do so when undesirable transgene silencing is encountered in transgenic plant given the teaching of Brigneti et al. that expression of silencing suppressor can release the transgenes from being silenced (abstract).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

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obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32-35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of U.S. Patent No. 6,632,980 in view of Brigneti et al. (1998, The EMBO Journal 17:6739-6746).

The claims are drawn to a binary transgenic viral expression system comprising 1) a chromosomally integrated blocking fragment bounded by site-specific sequences responsive to a site-specific recombinase; and 2) a chromosomally integrated inactive silencing suppressor transgene; wherein expression of the site specific recombinase results in the site-specific recombination that activates the silencing suppressor gene.

The patented claim is drawn to a binary transgenic expression system comprising: 1) a chromosomally integrated inactive replicon that insert into a reporter gene and contain cis-acting viral element, a target gene with at least one regulatory sequence and a site-specific sequence responsive to a site-specific recombinase; 2) a chromosomally integrated chimeric transactivating gene comprising a regulated plant

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promoter operably linked to a site-specific recombinase; wherein expression of the recombinase results in site-specific recombination which releases the inactive replicon (considered as a blocking fragment in instant claims) from the chromosome, activates replicon replication, increase expression of target gene and activates reporter gene.

The patented claim does not teach the silencing suppressor genes such as PI-HC-Pro, HC-Pro or 2b protein.

Brigneti et al. teach that HC-Pro polypeptides of TVY and 2b protein of Cucumber Mosaic Virus suppress the post transcriptional gene silencing and allow expression of GFP in the cell (abstract).

It would have been obvious to a person with ordinary skill in the art to modify the construct of the patented claims by using nucleotide sequence encoding 2b protein of CMV of Brigneti et al. as reporter genes, resulting the instant claims. One would have been motivated to do so given the teaching of Brigneti et al. that expression of silencing suppressor can release the transgenes from being silenced (abstract), and expression of a transgene of interest is desirable in the art.


Conclusion

Claims 32-36 are rejected. However, claims 33, 34 and 36 are free of prior art due to the failure of the prior art to teach or fairly suggest the inaction viral replicon as blocking sequence and BL1 or BR1 as silencing suppressors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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PRIMARY EXAMINER